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SUMMARY OF THESIS*

IGLÉZIAS, Silvia D'Andretta - Endomiocardiofibrose: patologia e correlação clínica em material de ressecção cirúrgica. São Paulo, 2007. (Tese de Doutorado - Faculdade de Medicina da Universidade de São Paulo).

ENDOMYOCARDIAL FIBROSIS: PATHOLOGICAL FINDINGS IN SURGICAL SPECIMENS AND CLINICOPATHOLOGICAL CORRELATION

BACKGROUND: Endomyocardial fibrosis (EMF) is a restrictive cardiomyopathy of unknown etiology prevalent in tropical regions. The disease involves the inflow tract and apex of either one or both ventricles and is characterized by a fibrous thickening of the endocardium and the underlying myocardium. Although its etiology remains unknown, most authors believe it could be related to systemic or heart infection/parasitism, previous blood eosinophilia or malnutrition. Surgical resection of the thickened endocardium is recommended to patients with advanced heart failure of functional class III or IV, New York Heart Association (NYHA). The gross and histological features of the heart have been comprehensively studied in autopsies and endomyocardial biopsies. Studies in surgical samples, however, are still lacking. **AIMS:** This study was conducted to evaluate: (1) the histomorphological changes of EMF as seen in surgical specimens by means of routine histological and immunohistochemical methods in an attempt to correlate them with clinical symptoms and coronary angiographic features; (2) to compare histological data between surgical and autopsy samples, and (3) to discuss probable pathogenetic mechanisms of the disease, as well as to investigate cardiotropic infective agents by means of molecular analysis of endomyocardial surgical samples. **METHODS:** We collected all available clinical records and endomyocardial surgical samples from 31 patients with EMF who had been submitted to surgery between 1991 and 2005 at InCor. The diagnosis was based on clinical, hemodynamic and angiocardiographic findings. The surgical samples were fixed in 10% formalin, submitted to standard processing, and stained with H&E, Masson's trichrome, reticulin and elastic stains. Immunohistochemical methods were employed to detect collagen fibers type I, II, and IV, inflammatory cells (CD3, CD20, CD68) and lymphatic vessels' endothelium (D2-40). Nine samples from autopsied hearts of EMF patients were used as a positive control group. Polymerase chain reaction (PCR) and reverse transcription-PCR were used retrospectively to search for genomes of *T. gondii* and cardiotropic viruses (enterovirus,

adenovirus, influenza A and B, cytomegalovirus, parvovirus B19 and herpes simplex) in the surgical material. All clinical and surgical reports were reviewed, including follow-ups and 16 coronary cineangiocardiographies. **RESULTS:** Ventricular endocardium was thickened by superficial acellular hyaline collagen fibers type I and III. Type-IV collagen fibers were seen only around vessels. Focal chronic inflammatory infiltrate with T-lymphocytes, macrophages and a few B-lymphocytes was seen around blood vessels with a peculiar pattern of vascular changes and numerous lymphatics within the endocardium. The superficial myocardium showed borderline myocarditis (Dallas criteria). RNA and DNA were successfully extracted from 12/36 samples. Infective agents were detected in 6/12 (50%) patients; two of them were positive for cytomegalovirus (CMV), two for enterovirus (EV), one for both (CMV and EV) and one for *T. gondii*. No histopathological differences between surgical samples and autopsy fragments were observed. Vascular blush or neovascularity was detected in nine of the 16 coronary cineangiocardiographies reviewed. Clinicopathologic characteristics are associated neither with infective genomes in the endocardium nor with vascular blush. **CONCLUSIONS:** Results indicate that there is a non specific chronic inflammatory process maintained by an anomalous vascular net rich in lymphatics situated deep within the endocardium. This angiolymphatic web probably contributes to the maintenance of the fibrotic plaque and might be considered an important pathological finding concerning in the pathogenesis of EMF. Histopathological changes as seen in surgical material are diagnostic of EMF. Molecular analysis of the endomyocardium revealed high incidence of cardiotropic infective agents, but their role in the pathogenesis of the disease is still controversial.

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